

Serial No. 09/361,542
P&G Case No. 7247M
Page 4 of 7

REMARKS

Claims 36, 38-39, 41-46, and 48 remain in the present application. Claims 1-35 and 40 have been previously canceled. Claims 37 and 47 are canceled. No additional claims fee is believed to be due.

Claims 36 and 43 have been amended to incorporate the citric acid limitation of canceled Claims 37 and 47, respectively.

Claim 48 has been amended to depend from Claim 43 rather than from canceled Claim 47.

Invention Synopsis

The present invention is directed to oral, liquid, aqueous, muco-retentive compositions, and a method of administering such compositions, wherein the compositions comprise colloidal particles of silicon dioxide, a select pharmaceutical active, and a citric acid.

It has been found that prolonged and improved coating and protection of components of the alimentary canal such as the stomach, esophagus, and small intestine can be achieved by incorporating a mucoadhesive material into an oral pharmaceutical composition. Unlike conventional mucoadhesive materials such as mucoadhesive polymers, the compositions of the present invention comprise a silicon dioxide which provides for highly effective mucoadhesive systems. It has also been found that when the compositions of the present invention comprise a citric acid, the solid particles of these highly effective mucoadhesive systems are consistently dispersed to result in improved stability of the systems.

Art Rejections

a) Rejection under 35 U.S.C. 102 over Boltri et al.

Claims 43-45 have been rejected under 35 U.S.C. 102 as being anticipated by Boltri et al. (EP 733,357). The Examiner contends that Boltri et al. disclose an aqueous liquid composition as claimed by Applicant, wherein the composition comprises colloidal silicon dioxide and a pharmaceutical active. Applicant respectfully traverses this rejection as it would apply to the amended claims.

Boltri et al. disclose aqueous pharmaceutical formulations which are in the form of thixotropic gels, and which comprise a pharmaceutical active and colloidal silica gelling agent. The pharmaceutical formulations of Boltri et al. are described as those pharmaceutical formulations that are suitable for topical, vaginal, nasal, and otological administration. Boltri et al., however, fail to disclose *oral*, aqueous pharmaceutical formulations, and certainly fail to disclose *oral*, aqueous pharmaceutical formulations comprising a citric acid.

Applicant submits that the Boltri et al. reference fails to anticipate Applicant's Claims 43-45, as amended, because this particularly applied reference fails to teach an oral, muco-retentive, aqueous liquid, pharmaceutical composition. Boltri et al. further fail to teach each and every limitation recited in the oral, muco-retentive, aqueous liquid, pharmaceutical composition of Applicant's Claims 43-45, as amended, wherein these amended claims are now limited to the composition comprising colloidal particles of silicon dioxide, a select pharmaceutical active, and a citric acid.

Serial No. 09/361,542
P&G Case No. 7247M
Page 5 of 7

In view of the foregoing remarks, it is submitted that the Boltri et al. reference fails to teach *oral* pharmaceutical compositions or each and every limitation recited in the *oral* pharmaceutical composition as claimed by Applicant. Therefore, the Boltri et al. reference fails to anticipate Applicant's Claims 43-45, as amended. Accordingly, the rejection of these claims as being anticipated by Boltri et al. is improper, and should be withdrawn.

b) Rejection under 35 U.S.C. 103 over Boltri et al.

Claims 43-48 have been rejected under 35 U.S.C. 103 as being unpatentably obvious over Boltri et al. (EP 733, 357). The Examiner contends that despite Boltri et al.'s failure to disclose an oral composition comprising citric acid, it would have been obvious to realize Applicant's invention based on Boltri et al.'s disclosure of pharmaceutical formulations comprising optional pharmaceutical excipients such as surfactants, preservatives, flavouring agents, co-solvents, and lipophilic phases. Applicant submits that Claim 47 has been canceled without prejudice, thus obviating this rejection as it would apply to this claim. Applicant respectfully traverses this rejection as it would apply to remaining amended Claims 43-46 and 48.

Boltri et al. disclose aqueous pharmaceutical formulations which are in the form of thixotropic gels, and which comprise a pharmaceutical active, colloidal silica gelling agent, and optional excipients such as surfactants, preservatives, flavouring agents, co-solvents, and lipophilic phases. The pharmaceutical formulations of Boltri et al. are described as those pharmaceutical formulations that are suitable for topical, vaginal, nasal, and otological administration. Boltri et al., however, fail to disclose *oral*, aqueous pharmaceutical formulations, and certainly fail to disclose *oral*, aqueous pharmaceutical formulations comprising a citric acid.

Applicant submits that the Boltri et al. reference would not obviously lead the skilled artisan to a realization of Applicant's invention of Claims 43-46 and 48, as amended. Boltri et al. fail to teach or suggest an oral pharmaceutical composition, and such composition comprising a citric acid. Boltri et al. teach and suggest pharmaceutical compositions that are suitable for topical, vaginal, nasal, and otological administration, and that comprise a pharmaceutical active and colloidal silica. By contrast, Applicant's amended Claims 43-46 and 48 are now limited to an oral, mucorectentive, aqueous liquid, pharmaceutical composition comprising colloidal particles of silicon dioxide, a select pharmaceutical active, and a citric acid.

The Examiner contends that it would have been prima facie obvious to realize Applicant's invention of remaining Claims 43-46 and 48 based on the teachings of the Boltri et al. reference, notwithstanding Boltri et al.'s failure to disclose *oral* pharmaceutical compositions and such compositions comprising citric acid or a salt thereof. The Examiner further contends that Boltri et al.'s disclosure of some known optional pharmaceutical excipients would lead the skilled artisan to search a document such as the International Cosmetic Ingredient Dictionary and Handbook for a citric acid pharmaceutical excipient. Applicant disagrees.

Serial No. 09/361,542
P&G Case No. 7247M
Page 6 of 7

Applicant submits that for an establishment of prima facie obviousness, three basic criteria must be met: 1) there must be some suggestion or motivation, either in the references themselves or in the knowledge generally available to one of ordinary skill in the art, to modify the reference or to combine reference teachings, 2) there must be a reasonable expectation of success, and 3) the prior art reference must teach or suggest all claim limitations. The applied Boltri et al. reference fails to teach or suggest an *oral* pharmaceutical composition as claimed by Applicant, or such a composition comprising all of the limitations of Applicants Claims 43-46 and 48, as amended. Accordingly, the applied Boltri et al. reference fails to meet the three basic criteria needed to render Applicant's Claims 43-46 and 48, as amended, unpatentably obvious based on prima facie obviousness.

Applicant further submits that since Boltri et al. teach and suggest optional pharmaceutical excipients such as surfactants, preservatives, flavouring agents, co-solvents, and lipophilic phases, this particularly applied reference may provide the motivation for the skilled artisan to seek a reference for known surfactants, preservatives, flavouring agents, co-solvents, and lipophilic phases, not a reference that teaches or suggests citric acid or a salt thereof, and certainly not exemplary "pH adjusters" as the Examiner suggested the skilled artisan would seek based on the optional pharmaceutical excipients disclosed by Boltri et al. Moreover, The Examiner has applied this obviousness rejection based on Boltri et al., then Boltri et al. should teach or suggest the oral, muco-retentive, aqueous liquid, pharmaceutical composition as claimed by Applicant.

In view of the foregoing remarks, it is submitted that the Boltri et al. reference fails to teach or suggest an oral, muco-retentive, aqueous liquid, pharmaceutical composition as now recited in Applicant's Claims 43-46 and 48. Rejection of these claims, as amended, as being unpatentably obvious over Boltri et al. is improper and, therefore, should be withdrawn.

c) Rejection under 35 U.S.C. 103 over Gallopo et al.

Claims 36-39 and 41-42 have been rejected as being unpatentably obvious over Gallopo et al. (U.S. Patent 4,915,948). The Examiner contends that based on the teachings of Gallopo et al. of orally administered pharmaceutical tablets, that it would have been obvious to formulate as well as administer an oral pharmaceutical composition as claimed by Applicant, wherein the oral pharmaceutical composition comprises colloidal silica particles, active agent, and citric acid. Applicant submits that Claim 37 has been canceled without prejudice, thus obviating this rejection as it would apply to this claim. Applicant respectfully traverses this rejection as it would apply to remaining amended Claims 36, 38-39, and 41-42.

Gallopo et al. disclose pharmaceutical tablets which have bioadhesion properties to mucous membranes, and which comprise a biopolymer, a solid polyol, and an active agent including pharmaceutical actives. Gallopo et al. further disclose that the tablets may comprise optional excipients such as citric acid, in addition to describing optional vehicles such as colloidal silica particles. Gallopo et

Serial No. 09/361,542
P&G Case No. 7247M
Page 7 of 7

al., however, fail to disclose oral *aqueous* compositions, and certainly fail to disclose oral, *aqueous* mucoretentive compositions.

Applicant submits that the Gallopo et al. reference would not obviously lead the skilled artisan to a realization of Applicant's invention of Claims 36, 38-39 and 41-42, as amended, because the Gallopo et al. reference fails to teach or suggest a method of administering *aqueous* mucoretentive compositions. Gallopo et al. teach and suggest the oral administration of tablets which comprise water-soluble materials. By contrast, Applicant's Claims 36, 38-39 and 41-42 are directed to a method of administering an aqueous mucoretentive composition.

The Examiner contends that Applicant's invention of Claims 36, 38-39 and 41-42 are prima facie obvious in view of Gallopo et al. since Gallopo et al. teach and suggest orally administrable tablets that comprise colloidal silica particles, active agent, and citric acid. Applicant disagrees. Applicant submits that since Gallopo et al. fail to teach or suggest a method of administering an *aqueous* mucoretentive composition as claimed by Applicant, then this particularly applied reference fails to render Applicant's Claims 36, 38-39 and 41-42 unpatentably obvious, prima facie or otherwise.

In view of the foregoing remarks, it is submitted that the Gallopo et al. reference fails to teach or suggest Applicant's invention of Claims 36, 38-39 and 41-42, as amended, wherein these amended claims are directed to a method of administering an *aqueous* mucoretentive composition that comprises colloidal particles of silicon dioxide, a select pharmaceutical active, and citric acid or a salt thereof. The rejection of these claims as being unpatentably obvious over Gallopo et al. is improper and, therefore, should be withdrawn.

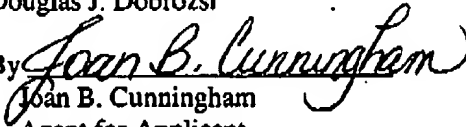
Conclusions

Applicant has made an earnest effort to place his application in proper form and to distinguish his claimed invention from the applied prior art. WHEREFORE, reconsideration of this application, withdrawal of the rejections under 35 U.S.C. 102 and 103, and allowance of Claims 36, 38-39, 41-46, and 48 are respectfully requested.

Respectfully submitted,

Douglas J. Dobrozsi

By


Joan B. Cunningham
Agent for Applicant
Registration No. 43,962
(513) 622-3993

August 27, 2003
Cincinnati, Ohio
Customer No. 27752